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ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

	G. R. Ewoldt, Ph.D.	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *4-8,10-13 and 18-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,9 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

Art Unit 1644

DETAILED ACTION

1. Applicant's election with traverse of Group II (an adjuvant or vaccine comprising IL15, or an IL15 homologue, and an anti-IL2 antibody), Claims 1-3, 9, and 14-17, filed 1/19/04, is acknowledged. Applicant argues that a search of Group II would include the subject matter of Groups I and III-XX. Applicant argues, "First, with regard to Groups I-XX, Applicants submit that a thorough search for Group II should also include the subject matter of Groups I and III-XX. In the present case, the subject matter of these Groups cited by the Examiner is sufficiently small and is so closely related as to be capable of examination together...Moreover, many of the groups appear to overlap given the manner in which they are divided. For example, comparing the election of IL-15 or a homologue thereof in Groups II, VII, XII, and XVII with the equivalent component in Groups I, VI, XI, and XVI (i.e., an agent that binds to an IL-15 receptor), it is submitted that IL-15 or a homologue thereof is an agent that binds to an IL-15 receptor, and therefore, given the overlap, it is improper to divide the claims on this basis."

These arguments are not found persuasive for the following reasons. "Independent and distinct" has been defined (as set forth in the MPEP) to encompass independent *or* distinct. Clearly a product and a method of its use are distinct inventions. While the search of a product and a method of its use may overlap, they are not coextensive. Whereas a product comprises only physical and structural limitations, a method of use encompasses numerous other limitations that might include time, dosage, etc. Regarding the various products, again, the searches may overlap but they are not coextensive. Accordingly, a showing of noncoextensive searches has been accepted by the Office as a showing a serious search burden on the Examiner. Also note that the restriction notes the linking nature of Claim 1.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 4-8, 10-13, and 18-51 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1-3, 9, and 14-17 read on the elected invention and are being acted upon.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 16-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed formulations would comprise effective vaccine formulations.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

Regarding a vaccine comprising the adjuvant formulation of the instant specification and an antigen, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable. The state of the vaccine arts are such that no formulations comprising an antigen, IL15, and an αIL2 antibody

that because vaccines are intended for *in vivo* therapy, i.e., the prevention or treatment of disease, the disclosure must be enabling for *in vivo* uses.

Regarding the claimed vaccine, the specification discloses just one relevant Example; in Example 3 it is shown that an anti-IL15R (anti-IL2Rβ) blocks the proliferation of T (presumably memory) cells while an anti-IL2R (anti-IL2Rα) increased said proliferation. Thus, *none* of the vaccines actually encompassed by the claims are disclosed. And particularly regarding anti-tumor vaccines and anti-HIV vaccines (i.e., "an infectious disease pathogen" particularly disclosed in the specification), significant enablement would be required for the following reasons.

While positive results have been achieved versus tumor associated antigens (TAAs) in some animal models, said achievements do not generally correlate with positive results in humans (i.e., the most likely intended subject for the claimed vaccines). As taught by Bodey et al. (2000) the reasons are relatively straight-forward:

"The theoretical basis for all of these approaches [immunotherapy] is very well founded. Animal models, albeit highly artificial, have yielded promising results. Clinical trials in humans, however, have been somewhat disappointing. Although general immune activation directed against the target antigens contained within the cancer vaccine has been documented in most cases, reduction in tumor load has not been frequently observed, and tumor progression and metastasis usually ensue, possibly following a slightly extended period of remission. The failure of cancer vaccines to fulfill their promise is due to the very relationship between host and tumor; through a natural selection process the host leads to the selective enrichment of clones of highly aggressive neoplastically transformed cells, which apparently are so dedifferentiated that they no longer express cancer cell specific molecules. Specific activation of the immune system in such cases only leads to lysis of the remaining cells expressing the particular TAAs in the context of the particular human leukocyte antigen (HLA) subclass and the necessary costimulatory molecules. The most dangerous clones of tumor cells however lack these features and thus the cancer vaccine is of little use."

Indeed this selection for the most aggressive tumor cells would likely exacerbate disease in the long run. At any rate, the reference demonstrates that significant enablement would be required for claims drawn to tumor vaccines.

Regarding formulations which induce effective anti-virally infected (i.e., "an infectious disease pathogen") cell immunity, even less is known. Indeed, as taught by Cohen (2002) it is not yet even known whether a CTL response against a virus such as HIV is even technically capable of providing effective immunity.

Other pathogens have proven just as difficult to vaccinate against, see for example Hagan et al. (2003) wherein it is taught that *Schistosoma* parasites resist even the most effective vaccines designed using the best characterized antigens. Indeed, once again the concept of antigen vaccination may not prove technically feasible given the finding that repeated exposure to the organism fails to induce protective immunity as happens with many viral and bacterial antigens (see particularly page 1273, column 1, second paragraph).

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, the breadth of the claims, and the lack of disclosure of *any* actual vaccines, it would take undue trials and errors to practice the claimed invention.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-3, 9, and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (1998, IDS) in view of Lenardo (1991, IDS).

Zhang et al. teaches that IL15 causes the "strong and selective" stimulation of memory T cells *in vivo* (see particularly the Summary).

The reference teaching differs from the claimed invention only in that it does not teach the use of IL15 in an adjuvant

Lenardo teaches that IL2 is required for the programmed cell death of mature (antigen activated) T cells (see particularly the Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a vaccine adjuvant comprising IL15 and an anti-IL2 antibody, given the combined teachings of Zhang et al. and Lenardo. One of ordinary skill in the art at the time of the invention would have been motivated to combine IL15 (because it stimulates memory T cells) and anti-IL2 antibody (because it would reduce the programmed cell death of the T cells stimulated by the IL15), to produce a vaccine adjuvant (i.e., a composition for increasing the immune response to an antigen) for the induction of an improved and long-lasting immune response.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

Please Note: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Primary Examiner
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